Modern Concepts of Cardiovascular Disease

Published monthly by the AMERICAN HEART ASSOCIATION

1790 BROADWAY AT 58TH STREET, NEW YORK, N. Y.

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VOL. XVI SEPTEMBER, 1947 No. 9

PARTICIPATION OF THE HEART IN SHOCK

Until recently, most investigators were agreed that the heart was little if at all injured by shock, no matter how elicited or prolonged. True, the evidence was not of a penetrating sort. Still, it showed that in most cases shock was not due primarily to failure of the heart. The extent of the injury to the heart, however, received slight attention.

Wiggers first presented evidence suggesting that the heart contributed to the circulatory failure of hemorrhagic shock. With Werle, he showed reduction of effective venous pressure did not account for the failure of cardiac output and arterial pressure in the majority of the animals studied. The capacity of the ventricles to respond to a given venous pressure, that is, to stretch, was reduced. In the remainder, decrease in systolic discharge was associated with a decrease in venous pressure and hence could be regarded as passive. Thus, reduced capacity of the myocardium to respond to a given venous pressure in some animals was suggested as one factor precipitating terminal or "irreversible" shock. The generally accepted view that the reduction of cardiac output after transfusion is due solely to reduction of venous return was not supported.

A year later Kohlstaedt and Page demonstrated a wide difference in response of different shocked dogs to intra-arterial transfusion. One group of animals tolerated large amounts of blood given rapidly without marked rise in intra-auricular pressure, while the other much smaller group responded differently. When a large volume of blood flowed in rapidly under a pressure of 50 mm. of mercury (the usual starting pressure for intra-arterial transfusion) and no corresponding immediate rise in arterial pressure occurred, circulatory failure with rise in intra-auricular pressure might be anticipated. It, therefore, seemed desirable to examine the responsiveness of the heart and peripheral vessels to pressor and depressor agents in shocked animals to ascertain whether the muscle of the vessel wall and the myocardium showed signs of injury. It soon became clear that shortly after eliciting burn shock, for example, often there was a phase of excitation when both the heart and blood vessels responded to chemical stimuli more actively than normal. This was followed by a depressed phase when they responded little or not at all. The latter phase corresponded to the terminal or "irreversible" state of shock.

Next, it was necessary to determine what effect changes in responsiveness had on the caliber of the peripheral vessels. This problem was not easy to settle because the trauma and exposure necessary in most experiments changed the responses unpredictably. It was for this reason that Page and Abell resorted to observation of the small vessels of rabbits' and cats' mesenteries and rabbits' ears protected by implanted Sandison-Clark chambers. While certain data, such as peripheral resistance, cannot be measured by this method, vasoconstriction and the rate and character of blood flow are accurately observable. Using these preparations it was shown that vasoconstriction occurred early in shock and persisted for prolonged periods but as the terminal nonreactive phase approached, dilatation replaced constriction. Loss of vascular responsiveness, therefore, was associated with loss of the ability to constrict.

Cardiometer studies with the closed chest method showed with regard to the heart that at first it shrinks down as if to adapt itself to reduced blood volume. Stroke volume, diastolic volume, venous and arterial pressure all declined sharply. But if the shock stimulus persisted, the time came when increases occurred in both systolic and diastolic volume. The rise in systolic volume was more rapid than in diastolic, hence stroke volume grew smaller as the dilatation progressed. Concurrently, heart rate decreased (Kohlstaedt and Page). The analogy of cardiac and peripheral vascular changes, namely, constriction followed by dilatation, is exact, and they tend to appear at the same times.

The coronary circulation is well known to be dependent on arterial pressure, more directly on the diastolic pressure. Unlike some other vascular areas of the body, these vessels seem to dilate as the pressure falls. Opdyke and Foreman found the flow decreased 30 to 60 per cent during periods of hypotension due to hemorrhage, although resistance to flow was greatly decreased. After transfusion of the removed blood, flow increased to 121 to 420 per cent of the control level. Consequently, coronary flow was almost invariably greater after hypotension and transfusion than at equivalent aortic pressures in the pre-shock state. Thus the cardiogenic aspect of shock probably has its origin in ischemia during the period of reduced coronary flow, but unlike the renal vasoconstrictive ischemia in shock (Corcoran and Page) this is abolished by restoration of blood volume. Prompt adequate transfusion is therefore a sure means of preventing cardiac damage in shock.

The electrocardiogram has not been of signal help in detecting the deleterious effects of shock. Thus Burnett, Bland and Beecher found no abnormal changes in twenty-five of thirty measurements made on patients with varying degrees of traumatic shock. It should be noted that the whole course of the shock was not followed. In animals electrocardiographic evidence of cardiac injury only becomes manifest late as Manrique and Proudfit and Glasser have found. Displaced S-T segments which became normal after transfusion and increased amplitude and sharpening of the T wave contour were observed repeatedly. Manrique noted that massage of the injured hind legs of a dog caused displacement of the S-T segment along with auricular and ventricular fibrillation.

The cause of damage to the heart during shock is not known. It is surprising how well it manages to overcome the serious obstacle of reduced blood supply for such long periods. But the defense mechanisms cannot be expected to hold off disaster indefinitely and the heart, just as the blood vessels, finally begins to show evidence of the ordeal to which it has been subjected.

Many changes in the content of blood have recently been demonstrated in shock, but it would

be futile at present to attempt to relate them directly to cardiac injury. An exception may be hyperpotassemia in crush syndrome.

Good chemical evidence exists that shock depletes the heart of substances necessary for its functioning. The amount of adenosine triphosphate, the energy source most directly coupled with function, is sharply reduced as are other substances, less directly connected with energy reservoirs such as phosphocreatine and glycogen (LePage). The decomposition of these reservoir materials initiates the glycolytic mechanisms leading to production of inorganic phosphate and lactic acid.

There is further evidence of widespread chemical disturbance, particularly as related to the important sodium ion. Gelhorn, Merrell and Rankin have shown that the exchange of sodium across the vascular membrane per unit of time is only about one half normal in shocked animals; and the exchange remains depressed immediately following replacement therapy with saline solution or serum. If the decrease in rate of movement of sodium across the vascular membrane is characteristic of other ionic species as well, it offers an illustration of the deep seated damage caused by shock. It is not surprising that the heart participates in this damage.

It is concluded that contrary to older beliefs, the heart, just as other portions of the vascular tree, suffers during prolonged periods of shock. Fortunately, the devices used by it to protect itself are usually adequate even under markedly adverse conditions. But clear evidence shows that protection does not last indefinitely and cardiac damage may contribute to the failure to respond to treatment.

Treatment

One fact has become clear. The longer the subject is allowed to remain untreated, the greater the danger of the occurrence of the terminal refractory phase. So far, no one has been able to restore all victims in this phase to health. On the other hand, many more animals in severe shock have been rescued by more nearly adequate treatment than had formerly been thought possible.

Since time is a matter of such importance, replacement of the blood into an artery instead of a vein is useful when shock is severe. When the arterial pressure is not less than 80 mm. of mercury, intravenous transfusion ordinarily suffices. But when it is lower than this, no time can be lost.

My associates and I have employed the femoral, dorsalis pedis and radial arteries as the vessels of choice. The latter two are cannulated and clotting is prevented by periodic washing out through a side arm with a solution of heparin. Blood, plasma or even saline solution are given from a reservoir bottle under a fixed air pressure generated by a rubber blast bulb. The pressure in the reservoir is usually set 20 to 30 mm. of mercury above the systolic level in the patient and blood is allowed to flow in until equilibration between the arterial contents and reservoir has occurred. The pressure in the reservoir is again raised in increments of 20 mm. or more until the desired blood pressure in the patient, usually 100 mm. of mercury, is achieved.

By taking serial x-ray pictures after injection of radiopaque medium into an exsanguinated dog, Glasser and Page found that fluid flows retrograde up the aorta filling the kidneys first, then the coronary and medullary vessels. Thus both the heart and vital centers of the medulla early receive oxygenated blood without the blood's having to traverse the lesser circulation before becoming available to the tissues. The pressure in the reservoir acts as a secondary heart to provide blood quickly and effectively to those organs most in need of it. It should be emphasized that this is only necessary when shock has advanced or is advancing rapidly.

But since this is the stage in which refractoriness to stimuli is becoming more marked and in which the heart is no longer actively adapting its size to the shrinking blood volume, but rather is dilating, an especial problem is created by the requirement of replacing the blood volume quickly. This is, of course, not a problem of the heart alone, but I shall limit discussion largely to it.

Kohlstaedt and Page found that 2-amino-heptane given into the tubing when the arterial transfusion was started seemed to prevent further dilatation in a heart already dilated. But Glasser and Page obtained better results in terms of survival when 0.25 mg. per 10 Kg. of body weight of ouabain was given. Administration of this cardiac glucoside seemed of significant value in dogs with terminal hemorrhagic shock by increasing the survival rate.

When the heart had stopped beating, administration of adrenalin into the transfusion fluid seemed to aid in restoring cardiac action and arterial pressure.

It is important not to overtransfuse either a patient or animal. Empirically, we have found that the mean arterial pressure should not be forced to more than 100 mm. of mercury. Marked cardiac irregularities and failure may be induced by overtransfusion; these are probably manifestations of the prior damage to the myocardium, which restoration of blood flow does not immediately relieve. In the recovery phase, it can no longer work at the high efficiency to be expected from a normal organ.

Nine years ago, Freeman, Shaffer, Schecter and Holling demonstrated that after total sympathectomy in dogs, even though the blood pressure was reduced to lower levels and for longer periods of time, shock was not produced. Dilution of the blood took place, there was prompt and beneficial reaction to blood transfusion, and the pathologic changes seen in the tissues of a non-sympathectomized animal in shock did not occur. The sympathectomized dogs, however, were unable to tolerate as large hemorrhages as normal dogs. In these reactions may lie the ability of sympathectomized dogs to withstand prolonged hypotension, that is, less ischemia of the tissues is produced. We were therefore interested to determine the effect of administration of tetra-ethyl ammonium chloride in animals subjected to severe hemorrhage. Acheson and Moe had shown that this drug paralyzes the autonomic ganglia, so blocking both sympathetic and parasympathetic impulses. Further, Page and Taylor found that the drug greatly augmented the action of a variety of pressor or depressor drugs, such as adrenalin, renin, angiotonin and barium chloride. The effect of tetra-ethyl ammonium chloride could be one of augmenting and maintaining the vascular and cardiac responsiveness to stimuli by chemical inhibition of the whole autonomic nervous system, so in part reproducing Freeman's results with the more limited sympathectomy. We found that injections of tetra-ethyl ammonium chloride prior to hemorrhage or even well after the hemorrhagic hypotension was established, not only restored and augmented the response to adrenalin but increased the survival rate.

With tetra-ethyl ammonium chloride treated animals, the amount of blood required to produce the same amount of hypotension as in normal dogs, was not significantly less. When the drug was given during the period of hypotension about 10 to 20 per cent of the withdrawn blood flowed back, only later to be forced out into the reservoir again in about thirty minutes. It appeared that the increased intake of blood is a factor but not the only one in increasing survival after prolonged hemorrhage.

It is of interest that Wiggers and associates have recently reported that dibenamine, a drug capable of lessening the vasoconstriction of shock, increased survival rate as well.

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